

Haemophilus influenzae type b diseases in Asia

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In Europe and North America, *Haemophilus influenzae* type b (Hib) disease was a major cause of mortality and morbidity among children under 5 years of age, with an estimated annual incidence of invasive Hib disease of 22–109 per 100 000 such children until the introduction of routine infant Hib immunization (1–4). Hib conjugate vaccine was extremely successful in nearly eliminating Hib diseases in countries where it was introduced for universal vaccination of infants (4, 5). It is therefore reasonable to ask whether such an effective vaccine should be introduced for routine infant immunization in other regions, such as Asia.

In a position paper on Hib conjugate vaccine, WHO recently made the following qualified statement: "In view of the demonstrated safety and efficacy of the Hib conjugate vaccines, Hib vaccine should be included, as appropriate to national capacities and priorities, in routine infant immunization programmes" (6). This statement highlights the two major barriers to the implementation of routine infant Hib immunization in Asia: the cost of Hib vaccine and its administration, which has to be accommodated by "national capacities"; and the absolute disease burden of Hib diseases and its relative burden in the broader context of total disease burden, which will determine the "national priorities".

The review by Peltola on pp. 878–887 of this issue of the *Bulletin* attempts to address the second of these barriers in the Asian context. This is a laudable undertaking, but is inherently difficult because of the relative dearth of quality data compared with what is available in industrial countries, as well as the enormous heterogeneity in Asia; both these conspire to make generalizations difficult. Two of the published population-based and prospective studies from China and Israel cited by Peltola report the incidence of Hib meningitis as about 10 and 22 per 100 000 children aged under 5 years,

respectively (7, 8). Other studies quoted by Peltola indicate that the incidence of Hib meningitis in the Middle East was about 13 to 22 per 100 000 children aged under 5 years; however, in East Asia, the corresponding incidence seemed to be lower at about 5 to 10 per 100 000 children aged under 5 years. The relatively high incidence of 50–66 per 100 000 children aged under 5 years in India quoted by Peltola is not even an estimate, but a proposal only (9). Similarly the incidence of Hib meningitis of 38 per 100 000 children cited by Peltola for Malaysia is an estimate based on hospital studies with only 16.3% of the meningitis cases having had a lumbar puncture (10). Therefore, based on current data, it is difficult to justify the overall incidence of 25 per 100 000 children for Hib meningitis in the whole of Asia quoted in Peltola's review, considering that the majority of the inhabitants live in East and South-east Asia. It is vital, therefore, that prospective population-based studies be conducted in Asia or that vaccine trials, along the lines of a trial conducted in the Gambia (11), be carried out to estimate the burden of Hib disease. Otherwise, there will be continuing confusion and plenty of excuses for policy-makers not to take Hib conjugate vaccine seriously. Better documentation of burden of disease is not just of academic interest but indispensable as part of a very complex strategy to introduce novel but relatively expensive vaccines, such as Hib and pneumococcal conjugate vaccines (12). Other components of the strategy include reducing the cost of the vaccines, effective advocacy, cost-effectiveness analysis, etc. (12). However, all these components ultimately depend on the reliable estimation of burden of disease. These estimates can then be used to calculate the cost of the immunization programme per death prevented and per disability-adjusted life year (DALY) for each country and economic stratum (13).

Of course it could be argued that the cost and time required for burden of disease studies would be prohibitive for most countries in Asia; hence the decision of whether or not to introduce routine infant immunization of infants with Hib vaccine has

to be based on whatever data are available. Currently, the high-income countries in Asia should address this issue of whether or not to introduce routine Hib immunization of infants because their "national capacities" could easily accommodate the cost of the vaccine and its administration; and even if the incidence of Hib disease in these countries is low, the benefits of such routine immunization could be substantial because the indirect medical costs and long-term treatment costs of Hib morbidity increase with per capita gross national product (GNP) (13). For example, in Hong Kong Special Administrative Region of China, where the estimated incidence of invasive Hib disease is only ca. 3 per 100 000 children aged under 5 years (14, 15), there would still be about 10–15 cases per year, with perhaps 2–3 children suffering sustained permanent neurological sequelae but surviving for decades, and thus in need of long-term health care. The net Hib immunization programme cost of US\$ 0.8 million for Hong Kong Special Administrative Region of China estimated by Miller (13) could easily be offset by the savings made in not having to provide care for these handicapped children for the rest of their lives. However, for low-income countries, the absolute cost involved will be high enough to prohibit implementation of routine Hib infant immunization, despite the demonstrated cost-effectiveness of such programmes (12, 13).

As far as relative burden of disease is concerned, there is no doubt from the data currently available that Hib is indeed a very important, if not the most important, etiological agent of childhood bacterial meningitis in Asia. This is clearly underlined in Peltola's review and should add weight to the argument that high-income countries in Asia should start to consider implementing routine immunization of infants with Hib vaccine.

Bacteraemic and nonbacteraemic pneumonia due to Hib should be included in moves to advocate routine infant immunization against Hib disease. However available data for Hib pneumonia with or without bacteraemia in Asia show that the numbers involved are even less than for meningitis.

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Peltola's review notes that Hib accounted only for a small proportion (2–3%) of bacteraemia in Bangladesh, Hong Kong Special Administrative Region of China, and Kuwait, compared with the much higher proportion (30–40%) in industrialized countries before routine infant immunization started (14). This would again argue indirectly that the incidence of Hib disease in Asia is lower than that in the pre-vaccination era in industrialized countries. For Hong Kong Special Administrative Region of China, pneumococci accounted for 22% of cases of sepsis in infants and preschool children, while *H. influenzae* accounted for only 2% (16). This in turn suggests that the burden of sepsis due to pneumococci could be ten times that of Hib. With the advent of pneumococcal conjugate vaccine, one would hope that the scientific community is now better prepared to estimate accurately the pneumococcal disease burden, which seems to be much more substantial than that of Hib (17). Nevertheless, for the low-to-middle income countries in Asia, the major barrier to routine infant immunization against Hib or pneumococci could still be their inadequate "national capacities". ■

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